"For example, some examples of suitable contact lens materials, include, but are not limited to, the polymeric materials disclosed in U.S. Patent No. 5,760,100 to Nicolson et al., which is incorporated herein by reference". [Emphasis added]

On page 7, lines 19-23, Applicants also state:

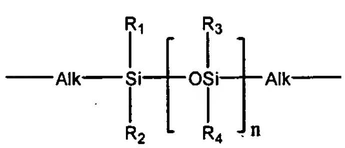
"According to one embodiment of the present invention, a polycationic material is combined with a polyanionic material to form a "single-dip" polyionic solution as set forth in U.S. Patent Application Serial No. 60/180,463 described above, which is incorporated herein in its entirety by reference thereto." [Emphasis added]

U.S. Patent Application Serial No. 60/180,463 is the parent of the U.S. Patent Application Serial No. 09/775,104 filed February 1, 2001 which published December 6, 2001 with Publication No. 20010048975A1.

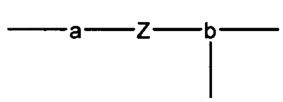
On page 70, lines 16-18, Applicants further states

"The macromonomers of formula (1) may be prepared by methods, for example as described in WO 99/57581 which has been incorporated herein by reference." [Emphasis added]

Those documents as parts of the original filed disclosure provide supports for the structural formula as follows:

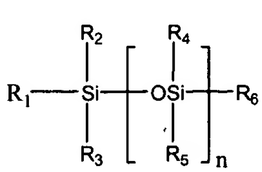


is disclose in and supported by U.S. Patent No. 5,760,100 (col. 21, lines 40-45) and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0107**).



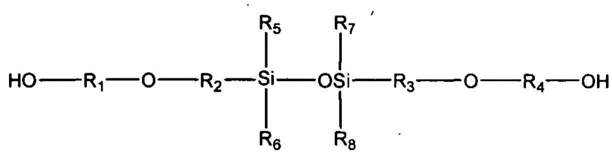
(II)

is disclose in and supported by U.S. Patent No. 5,760,100 (col. 28, lines 45-60) and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0118**).



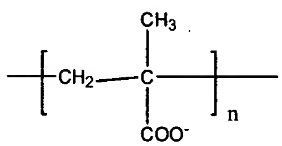
(IV)

is disclose in and supported by U.S. Patent No. 5,760,100 (col. 29, lines 15-20) and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0133**).

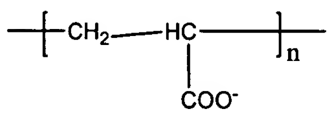


(V)

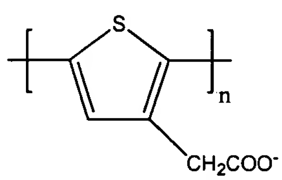
is disclose in and supported by U.S. Patent No. 5,760,100 (col. 40, lines 25-30) and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0140**).



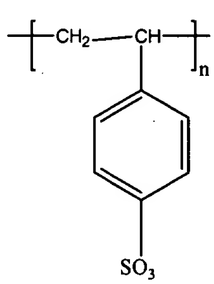
represents polymethacrylic acid and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0039**).



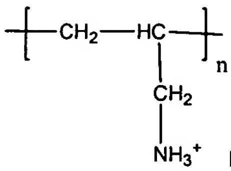
represents polyacrylic acid and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0038**).



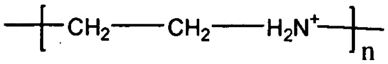
represents poly(thiophene-3-acetic acid) and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0040**).



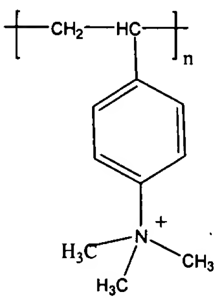
represents poly(4-styrenesulfonic acid) and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0041**).



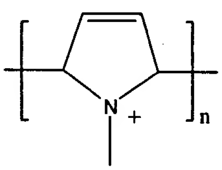
represents poly(allylamine hydrochloride) and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0031**).



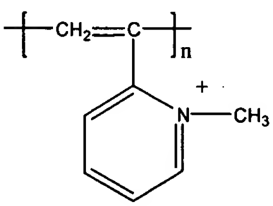
represents poly(ethyleneimine) and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0032**).



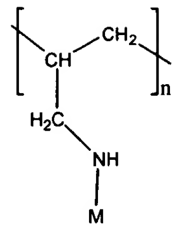
represents poly(vinylbenzyltriamethylamine) and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0033**).



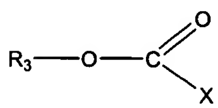
represents polypyrrole and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0035**).



represents poly(pyridinium acetylene) and further supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0036**).

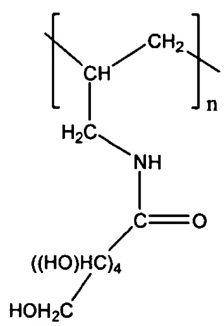


is disclosed in and supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0042**).

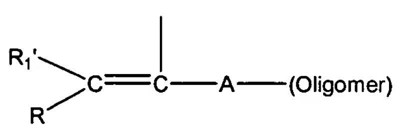


(6e)

is disclosed in and supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0051**).

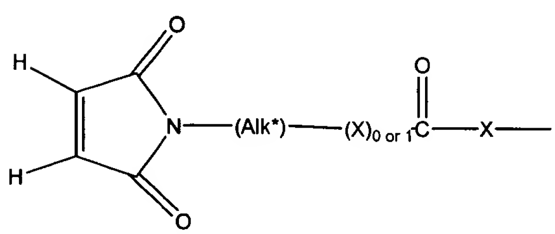


is disclosed in and supported by U.S. Patent Application publication No. 20010048975A1 (paragraph **0053**).



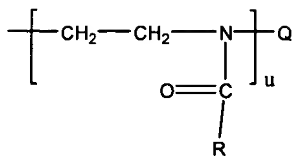
(1),

and



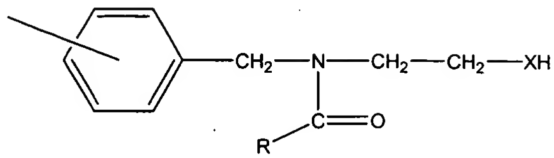
(2f),

are disclose in and supported by PCT Publication No. WO 99/57581 (page 2).



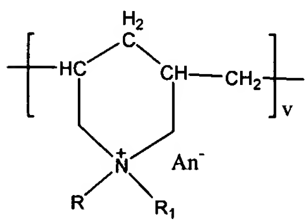
(3b),

and



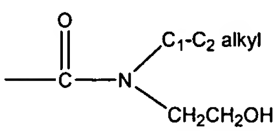
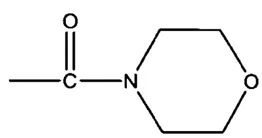
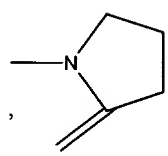
(3b'),

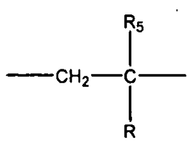
are disclose in and supported by PCT Publication No. WO 99/57581 (page 3).



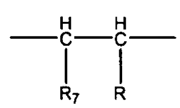
(3c),

is disclose in and supported by PCT Publication No. WO 99/57581 (page 4).


,

,

, is disclose in and supported by PCT Publication No. WO 99/57581 (the paragraph bridging page 20 and page 21).

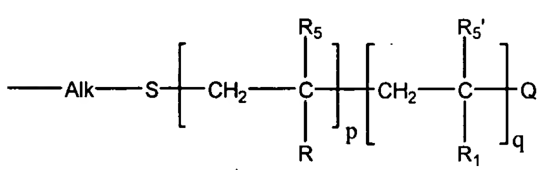


(4a) or

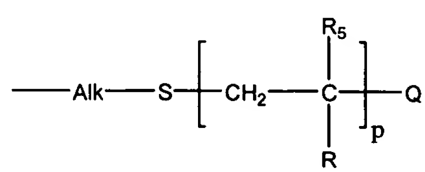


(4b),

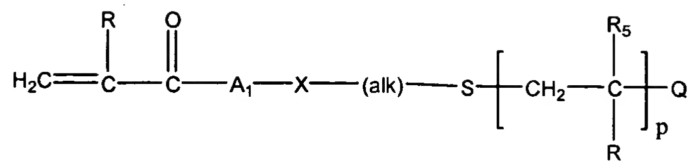
is disclose in and supported by PCT Publication No. WO 99/57581 (page 23).



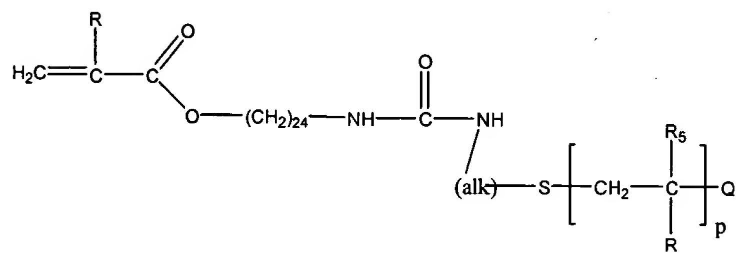
and



are disclose in and supported by PCT Publication No. WO 99/57581 (page 24).



and



are disclose in and supported by PCT Publication No. WO 99/57581 (page 25).

The second paragraph on page 71, lines 11-22, has been amended to correct typos and more clearly describe the invention. The phrase “a tie layer” should be “a hydrophilic layer” as clearly shown by the teachings from the third paragraph on page 45 to the second paragraph on page 71, lines 11-22, namely how to graft a coating having a so-called bottle brush-type structure (BBT) composed of tethered "hairy" chains, on top of a polymeric tie layer on the surface of a bulk material. Such grafting techniques is disclosed in detailed in WO 99/57581, which has been incorporated by reference in its entirety (the third paragraph on page 45). The second paragraph on page 71, lines 11-22, summarizes these teachings.

The first paragraph on page 72, lines 1-11 has been amended to correct typos and more clearly describe the invention. In the sentence “ When the outer coating is hydrophilic, such a tie layer is obtainable by grafting one or more hydrophilic monomers or macromonomers onto the surface, wherein the latter makes up at least 50 %, from about 75 to about 98 % and from about 80 to about 95 % of the total thickness of the fully hydrated coating", “a tie layer" should mean an outer coating which may be hydrophilic, preferably having a so-called bottle brush-type structure (BBT) composed of tethered "hairy" chains; and should be “it” or “the outer coating”, as clearly shown by the teachings in the paragraphs immediately preceding this paragraph (from the third paragraph on page 45 to the second paragraph on page 71, lines 11-22, namely).

Attached hereto is a marked-up version of the changes made to the **specification** by the present amendment. The attached page is captioned “Version With Marking To Show Changes Made.”

Claim Rejections Under 35 USC 112

Claims 1-13 and 17 were rejected under the 35 U.S.C. §112, first paragraph. The rejection over these claims is respectfully traversed for the following reasons.

Applicants respectfully submit that the phrase "polyionic material which is not covalently attached to the surface of the article" is fully supported by the originally-filed specification. For example, on page 18, the third paragraph, Applicants states:

> "Moreover, the material to be coated may also be an inorganic or metallic base material that, *prior to coating,* **does not contain any appropriate reactive groups**. no
> Examples of such base materials include ceramics, quartz, or metals, such as silicon or gold, or various non-reactive polymeric or non-polymeric substrates. Examples of such materials are employed in implantable biomedical applications, where ceramics are common, and in biosensor products, where gold, quartz, or other non-polymeric substrates are common." [Emphasis added]

The phrase "*prior to coating,* **does not contain any appropriate reactive groups**" clearly refers that no chemical reaction occurs to covalently attach the polyionic material(s) to the substrate material.

Support for this amendment also can be found in the teachings of the second paragraph on page 44, lines 4-9. The second paragraph on page 44 teaches how to obtain a tie layer in a process including (1) first swelling a substrate material in a solvent solution containing a solvent and at least one polyionic material material enlarges the scope of limitation and (2) then allowing the substrate material to shrink so that the substrate material entrap part or all of the initial layer of polycationic or polyanionic material. no

In addition, Examples A1, A2, F, H, I and J clearly teaches in detail that a polyelectrolytic tie layer is obtained by **physically depositing** (dipping in one or more polyionic material solutions) one or more polyionic materials onto the surface of a substrate. **No crosslinking agent** is present in the polyionic material solutions and **none** of polyionic material for forming the polyelectrolytic tie layer **contains any isocyanate (-N=C=O) or vinylic ($-CH=CH_2$) groups** which might react chemically with the functional groups (e.g., amino or hydroxyl groups), if available, on the surface of a contact lens to form covalent bonds.

Furthermore, Applicants has teaches and discloses in detail in a copending application 60/180,576 a contact lens forming process in which a coating of a polyionic material(s) is applied to a mold before forming a lens therein and then the coating is transferred to a contact lens formed within the mold. U.S. Patent Application No. 60/180,576 has been incorporated in its entirety by reference (page 8, lines 13-15) and is the parent of the U.S. Patent Application Serial No. 09/774,942 filed January 31, 2001 which published November 29, 2001 with Publication No. 20010045676A1. Such teaching clearly indicates that a layer of a polyionic material in a tie layer is

not covalent attached to the surface of the article, since it can be transferred from the mold surface to the contact lens surface.

no -bond can be broken

Applicants further submits that on page 72, in the sentence " When the outer coating is hydrophilic, such a tie layer is obtainable by grafting one or more hydrophilic monomers or macromonomers onto the surface, wherein the latter makes up at least 50 %, from about 75 to about 98 % and from about 80 to about 95 % of the total thickness of the fully hydrated coating", "a tie layer" was typos and should mean "an outer coating which is hydrophilic" in view of teachings immediately preceeding this paragraph. Examples E1-E6 further teach in detail how to obtain a hydrophilic outer coating on top of a polyelectrolytic tie layer on the surface of a contact lens. A tie layer is formed by depositing **polyionic materials** onto a substrate. On the paragraph bridging page 7 and page 8, Applicants state:

> "In accordance with the present invention, a coating process is provided that can be utilized to **deposit polyionic materials** onto a substrate to form polymeric tie layers having functional groups thereon so that additional active agents can be attached thereto. In one embodiment, for example, a process of the present invention allows the deposition of a bicomponent polyionic solution to a biomaterial substrate, such as a contact lens."

A tie layer is **not** obtained from **hydrophilic monomers or macromers**.

In sum, Applicants respectfully submit that the new claim limitation is fully supported by the originally-filed specification. Applicants respectfully request withdraw of the rejection under the 35 U.S.C. §112, first paragraph.

Rejections Under 35 USC 102(b)

Claims 1-2, 5-6, and 12-13 were rejected under 35 USC 102(b) as being anticipated by Nakagawa et al. (US Pat. 5,409,731). The rejection over these claims is respectfully traversed for the following reasons.

Examiner maintains the rejection by arguing that amino group-containing tie layer of Nakagawa is polyionic and is also merely "adsorbed" to the surface (col. 6, line 45). However, Examiner fails to note that in Nakagawa's method, after a contact lens "adsorbs" an amino group containing polymer thereon, "**and then** the contact lens is contacted with a solution containing a crosslinking agent to **crosslink** (i.e., covalently attach) the amino group-containing polymer on the contact lens surface to impart a hydrophilic nature to the contact lens" (col. 6, lines 46-50). Clearly, Nakagawa teaches that an amino group containing polymer is cross-linked to the surface of a contact lens with the help of a cross-linking agent. Therefore, Applicants submit that the claimed invention are not anticipated by Nakagawa, since the cited reference teaches a surface modification

only embod

no

or its self

what about when ref. teaches "adsorbed" at same time as x-link?

totally different from the present invention as currently claimed. Applicants respectfully request withdrawal of the 35 U.S.C. §102(b) rejection.

Claims 1-2, 5-6, and 12-13 were rejected under 35 USC 102(b) as being anticipated by Wilson (U.S. Pat. 6,050,980). The rejection over these claims is respectfully traversed for the following reasons.

Applicants submit that the polyisocyanate (i.e., hexamethylene diisocyanate) of Wilson is not a polyionic material as defined by Applicants in the specification. On page 7, in the third paragraph, Applicants state:

> "Typically, a polycationic material of the present invention can include any material known in the art to have a plurality of positively charged groups along a polymer chain, such as poly(allyl amine hydrochloride). Likewise, a polyanionic material of the present invention can typically include any material known in the art to have a plurality of negatively charged groups along a polymer chain, such as polyacrylic acid."

A polyionic material is a material that has a plurality of charged groups **along a polymer chain**. The polyisocyanate of Wilson is a croslinking agent and must contain at least two isocyanate groups (-N=C=O). The example given by Wilson is hexamethylene diisocyanate which definitively **is not** a polymer. Furthermore, isocyanate groups are extremely reactive toward hydroxyl groups (-OH), amine groups ($-NH_2$ or –NHR) and water. Wilson utilizes such high reactivity of isocyanate to attach covalently a layer of polyisocyanate with at least one unreacted isocyanate group onto a substrate as a tie layer which can further reacts with the functional groups of an antithrombic agent to form blood compatible surface coating. The tie layer is covalently attached to the surface of the lens. In addition, isocyanate (-N=C=O) groups are not cyano (-C≡O) groups. in contrast to the Examiner's assertion, **isocyanate groups are not ionic in nature**. Therefore, Applicants submit that the claimed invention are not anticipated by Wilson as discussed above. Applicants respectfully request withdrawal of the 35 U.S.C. §102(b) rejection.

exemplary polyisocyanate

what?

Rejections Under 35 USC 103(a)

Claims 1-6 and 12-13 were rejected under 35 USC 103(a) as being unpatentable over Takemura et al. The rejection over claims 1-6 and 12-13 is respectfully traversed for the following reasons.

Takemura teaches how to form a lubricating surface coating layer on a medical instrument. The lubricating surface coating layer of Takemura is formed by c **valently attaching** to the medical instrument a natural water-soluble polymer or synthetic water-soluble polymer, which can be a

to the 1st layer

polyionic material, for example, polyamines, poly-electrolytes, polystyrene sulfonate (col. 5, lines 4-7). The natural water-soluble polymer or synthetic water-soluble polymer is covalently bonded with a reactive functional group existing on or introduced in the surface of a substrate (col. 5, line 40-43). A reactive functional group can be introduced in the surface of a substrate by pre-treating the substrate with certain substances. Takemura states (col. 6, lines 29-37):

> "In these cases, the substrates are pre- treated with substances having a reactive functional group so that the reactive functional group may be present in or on the substrates, and the water-soluble polymer as specified by the present invention is covalently bonded therewith. The form of bond may include covalent bond, ionic bond, physical adsorption, etc. The covalent bond is most preferred in retention, although the ionic bond is allowable."

Takemura specifies examples of substances being used to pre-treat the substrate in col. 6, lines 44-52):

> "Examples of the substances having the reactive functional group include polyisocyanates such as ethylene diisocyanate, hexamethylene diisocyanate, xylene diisocyanate, toluene diisocyanate, diphenyl methane diisocyanate, naphthalene diisocyanate, phenylene diisocyanate, cyclohexylene diisocyanate, triphenylmethane triisocyanate, toluene triisocyanate, or the like; and adducts and prepolymers of these polyisocyanates with polyols."

Applicants submit that the substance described by Takemura **are not** polyionic materials by the definition of a polyionic material provided in the specification as discussed above. Those materials of Takemura are polyisocyanates. Polyisocyanates **are not ionic in nature**. Moreover, Takemura teaches that polyionic materials (e.g., water-soluble polymers having groups such as $-CONH_2$, $-COO^-$, $-NH_2$, $-SO^-_3$, and $-NR^+_3$; sodium polyacryalates; poly-electrolytes) are used to form a lubricating layer which is covalently attached to a substrate (col. 4, line 31 to col. 5, line 8). Takemura specifically states:

> "When these polymers are covalently bonded with a reactive functional group existing on or introduced in the surface of a substrate, a lubricating layer carried on the substrate can be obtained. The lubricating layer is not soluble in water and offer a lasting lubricating surface. The type of water-soluble polymer is not critical, but there can be mentioned, as typical examples, celluloses, maleic anhydride polymers, acrylamides, water-soluble nylons or the like. Among these, hydroxypropyl cellulose, methyl vinyl ether-maleic anhydride copolymer, polyacrylamide, and water-soluble nylon (AQ-nylon P-70 manufactured and sold by Toray Industries, Inc.) are easily available at a reasonable cost and excellent in safety." [Emphasis added]

Clearly, Takemura does not disclose or suggest anything about using of polyionic materials to functionalize the surface of an article in a non-covalent attachment manner. Applicants submit that,

since Takemura does not appreciate the present invention and since Takemura would not teach, suggest or motivate one skilled in the art to arrive at the present invention, a *prima facie* case of obviousness can not be established. Applicants respectfully request withdrawal of the 35 U.S.C. §103(a) rejection.

Claims 1-4, 6-13 and 12-13 were rejected under 35 USC 103(a) as being unpatentable over Vanderlaan et al. The rejection over claims 1-4, 6-13 and 12-13 is respectfully traversed for the following reasons.

In contrast to the Examiner's assertion, the cited reference (Vanderlaan et al.) teaches and discloses that hydroxyl or amino functionalities are incorporated into the surface by incorporating into the surface materials. Vanderlaan et al. state (col. 6, lines 48-61):

> "In the processes and devices of the invention, if the surface material to be coated does not contain the requisite functional group, such groups may be incorporated into **the surface material**. For example, hydroxyl groups may be incorporated by addition of one or more hydroxyl- containing monomers into the polymers used to form the surface. Examples of such hydroxyl containing monomers include, without limitation, mono(meth)acrylates of ethylene glycol, propylene glycol, glycerol, tetraethylene glycol, and the like. Amino groups may be incorporated using, without limitation, (meth)acrylates of aminoalcohols such as aminoethanol, tert-butylaminoethanol, or (meth)acrylamides of diamines such as bisaminopropane."
> [Emphasis added]

This paragraph clearly teaches that a hydroxyl or amino containing monomer is copolymerized with other material to form **the surface material**. Vanderlaan et al further teaches in detail in the working Examples about how to incorporate hydroxyl or amino functionalities into the surface through the use of the amine or hydroxyl functional monomer or macromers (col. 5, line 55 to col. 10, line 29). Those Examples clearly teach that the amine or hydroxyl functional monomer or macromers are copolymerized with other monomers or macromers to form surface material. Vanderlaan does not disclose nor suggest anything about using of polyionic materials to functionalize the surface of an article in a non-covalent attachment manner. Vanderlaan would not teach, suggest or motivate one skilled in the art to arrive at the present invention. Applicants submit that a *prima facie* case of obviousness can not be established and request withdrawal of the 35 U.S.C. §103(a) rejection.

CONCLUSION

For the foregoing reasons, Applicants submit that Claims 1-13 and 17 are patentable over the cited prior art. Applicant respectfully requests reconsideration and withdrawal of the claim objections and rejections set-forth in the Office Action and allowance of claims 1-13 and 17.

Should the Examiner believe that a discussion with Applicants' representative would further the prosecution of this application, the Examiner is respectfully invited to contact the undersigned. Please address all correspondence to Thomas Hoxie, Novartis Corporation, Corporate Intellectual Property, One Health Plaza, Bldg. 430, East Hanover, NJ 07936-1080. The Commissioner is hereby authorized to charge any other fees which may be required under 37 C.F.R. §§1.16 and 1.17, or credit any overpayment, to Deposit Account No. 19-0134.

Respectfully submitted,

Jian S. Zhou

Jian S. Zhou
Reg. No. 41,422
(678) 415-4691

Date: April 10, 2003

Novartis Corporation
Corporate Intellectual Property
One Health Plaza, Bldg. 430
East Hanover, NJ 07936-1080

V rsion with Markings to Show Changes Made

In th Specification:

E). Please amend the second paragraph on page 71, lines 11-22 as follows:

The grafting of such macromonomers to the bulk substrate material surface through attachment at the reactive sites of a polymeric tie layer ~~sites~~ yields a hydrophilic ~~tie~~ layer having for example a so-called bottle brush-type structure (BBT) composed of tethered "hairy" chains. Such BBT structures in one embodiment comprise a long hydrophilic or hydrophobic backbone which carries relatively densely packed comparatively short hydrophilic side chains (called primary bottle brushes). Another embodiment relates to secondary bottle brushes which are characterized in that the hydrophilic side chains themselves carry densely packed hydrophilic "secondary" side chains. Polymeric coatings of said primary and secondary BBT structures to a certain extent mimic highly water-retaining structures occurring in the human body, for example in cartilage or mucosal tissue.

F). Please amend the first paragraph on page 72, lines 1-11 as follows:

The complete coating of the bulk material according to the invention consists (a) of at least a partial tie layer, one or more tie layers comprising polyelectrolytes and (b) of an outer coating which may be hydrophilic or which may comprise various other active agents such as anti-microbial agents, organoselenium or block-type copolymers wherein one block is LbL active and the other is not. When the outer coating is hydrophilic, it ~~such a tie layer~~ is obtain~~abled~~ed by grafting one or more hydrophilic monomers or macromonomers onto the surface, wherein the latter makes up at least 50 %, from about 75 to about 98 % and from about 80 to about 95 % of the total thickness of the fully hydrated coating.